

**ABSTRACT OF THE DISCLOSURE**

Presenilin Associated Membrane Protein (PAMP), and nucleic acids encoding this protein, are provided. PAMP and *PAMP* nucleic acids provide diagnostic and therapeutic tools for evaluating and treating or preventing neurodegenerative diseases. In a specific embodiment, mutations in PAMP are diagnostic for Alzheimer's Disease or spina bifida. The invention further relates to screening, particularly using high-throughput screens and transgenic animal models, for compounds that modulate the activity of PAMP and presenilins. Such compounds, or gene therapy with PAMP, can be used in treating neurodegenerative diseases, particularly Alzheimer's Disease. In addition, the invention provides PAMP mutants, nucleic acids encoding for PAMP mutants, and transgenic animals expressing PAMP mutants, which in a preferred aspect result in biochemical changes similar to those induced by mutations in  $\beta$ APP, PS1, or PS2, associated with familial Alzheimer's disease.

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